The ATSDR Experience in Using the Supplemental Documents Database in Developing Toxicological Profiles

Henry G. Abadin, MSPH
ATSDR, Division of Toxicology
EPA Science Forum
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Toxicological Profiles

- **Succinctly characterize the toxicological and adverse health effects information**
- **Determine levels of exposure that present a significant risk to human health**
- **Identify research areas needed to fill data gaps**
- **Undergo independently peer-reviewed**
- **Made available for public comment**

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Tox Profile Contents

- **Public Health Statement (English and Spanish)**
- **Health Effects**
- **Toxicokinetics**
- **Mechanisms of Action**
- **Biomarkers**
- **Chemical/Physical Properties**
- **Production/Import/Use/Disposal**
- **Environmental Fate**
- **Analytical Methods**
- **Regulations/Advisories**
- **Identification of Data Needs**
- **Children's Health/PBPK/Reducing Toxic Effects/ Endocrine Disruption/Wildlife**

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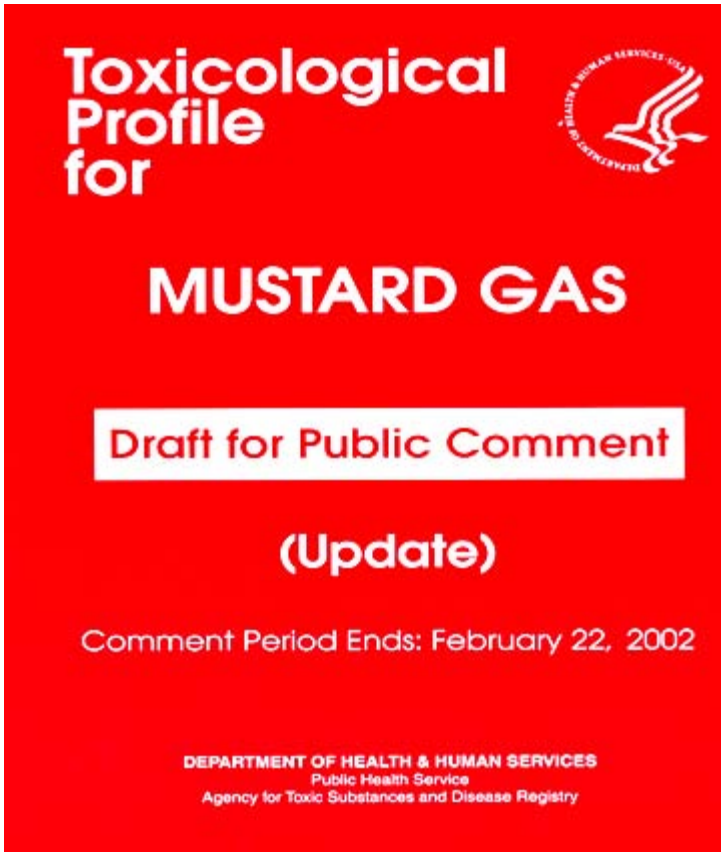
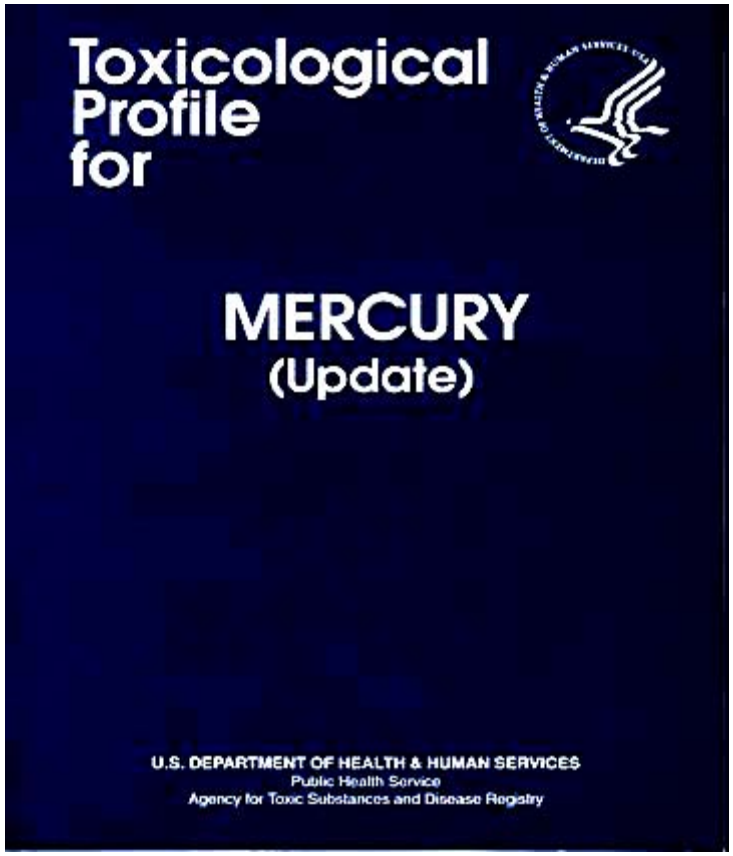

Toxicological Profile for
MUSTARD GAS
Draft for Public Comment
(Update)
Comment Period Ends: February 22, 2002
DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry


Toxicological Profile for
MERCURY
(Update)
U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Agency for Toxic Substances and Disease Registry

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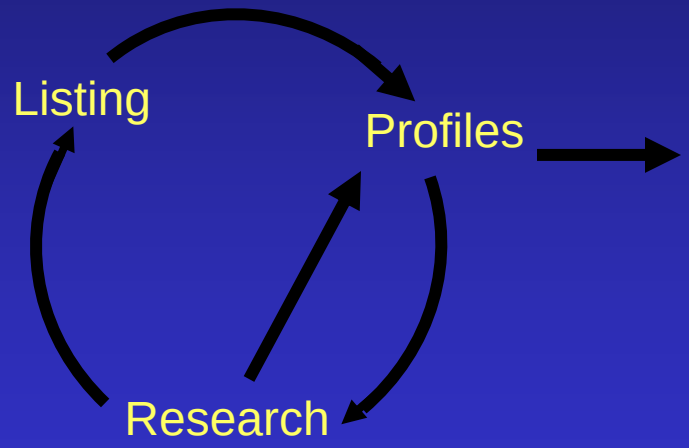
Role of Profiles in Public Health Practice



- ***Emergency Responses***
- ***Public Health Assessments***
- ***Consultations***
- ***Priority Health Conditions***
- ***Health Advisories***
- ***Environmental Alerts***

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Department of Energy

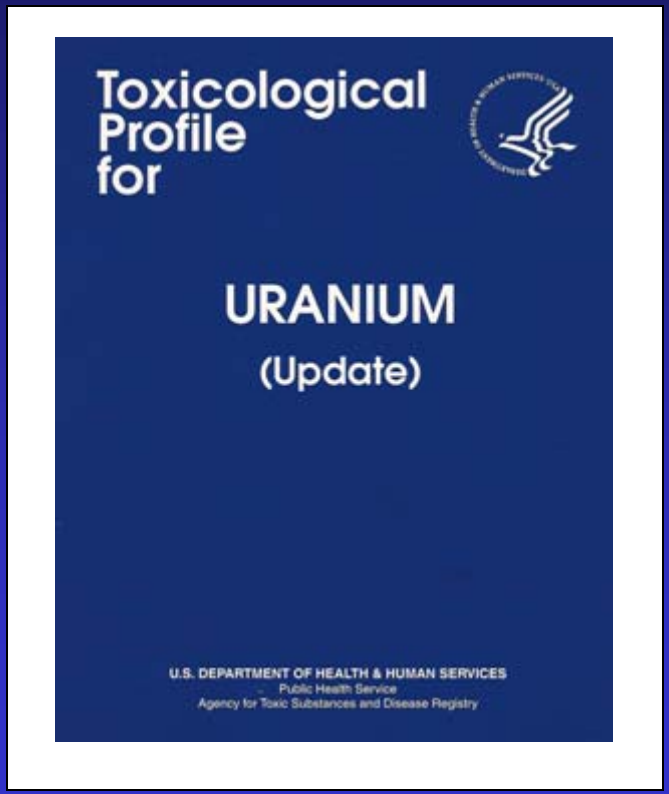
Section 104(i)(3) and (5) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980

Ionizing Radiation

Uranium

Americium
Cesium
Cobalt
Iodine
Strontium

Hanford Site



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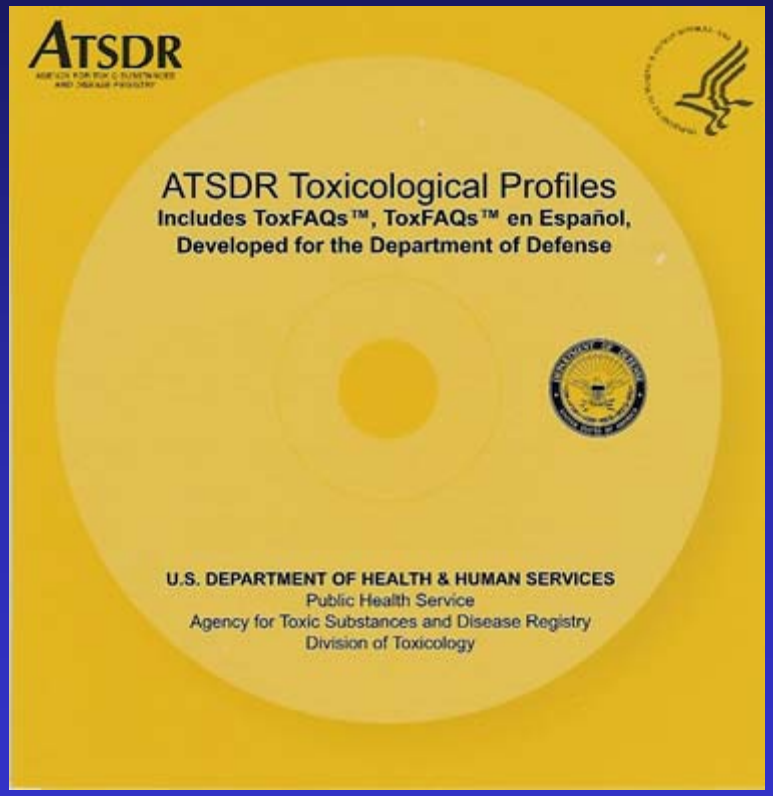
Department of Defense

Title 10 U.S.C., Section 2704(b)

1,3-DI / 1,3,5-TRINITROBENZENE
2,4,6-TRINITROTOLUENE
2-BUTOXY ETHANOL
DIETHYL PHTHALATE
DIMP
DI-N-OCTYLPHTHALATE
ETHYLENE / PROPYLENE GLYCOLS
FUEL OILS
GASOLINE
HEXACHLOROETHANE
HEXAMETHYLENE DIISOCYANATE
HMX
HYDRAULIC FLUIDS
HYDRAZINES
JET FUELS (JP-4 & JP-7)
JET FUELS (JP-5 & JP-8)
METHYLENEDIANILINE
MINERAL-BASED CRANKCASE OIL
OTTO FUEL II
RDX
STODDARD SOLVENT
TETRYL
TITANIUM TETRACHLORIDE
TOTAL PETROLEUM HYDROCARBONS
WHITE PHOSPHORUS



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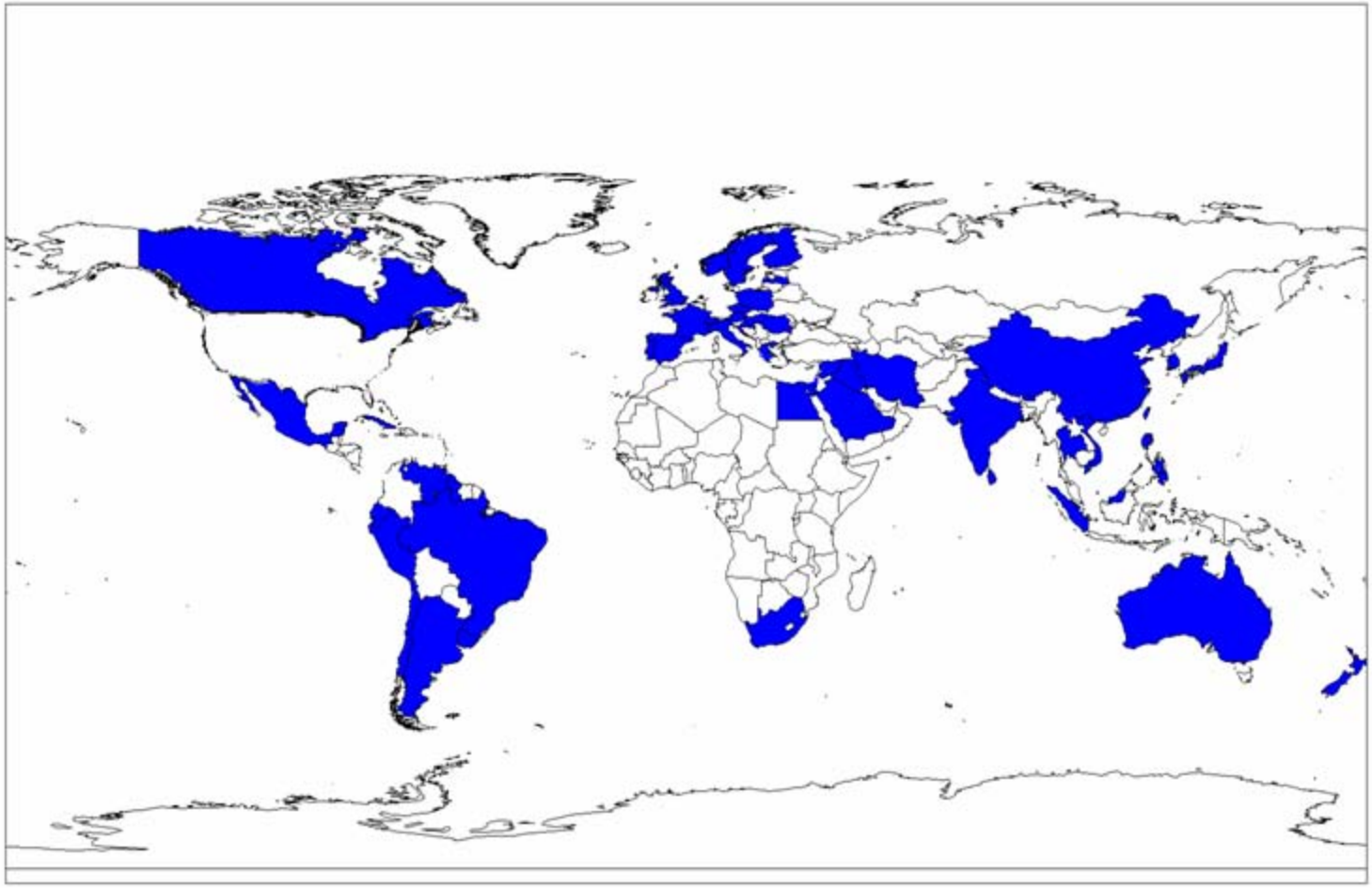
Tox Profile Distribution



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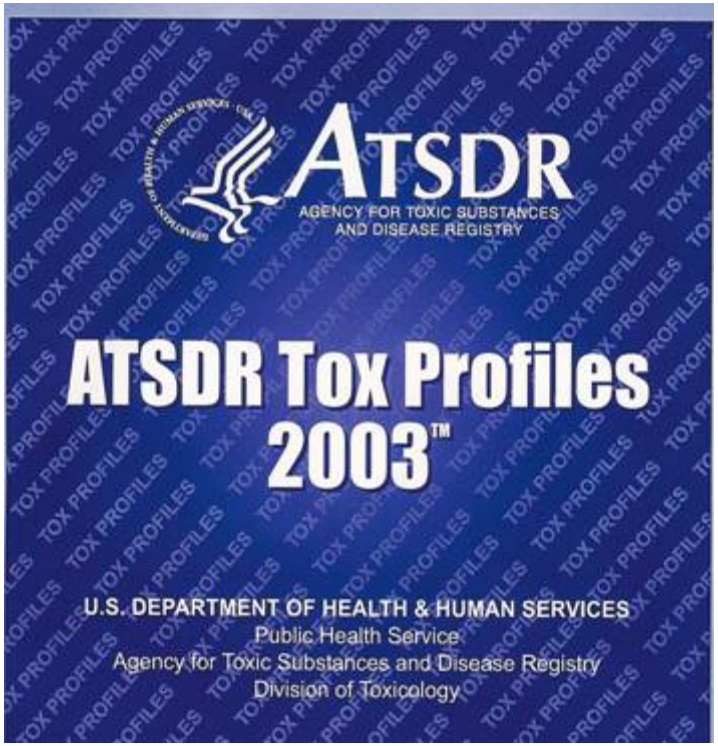
ToxProfiles 2003™ CD-ROM

- **161 Toxicological Profiles**
- **9 Interaction Profiles**
- **Navigation hyperlinks to easily locate information**
- **Full install capability to local drive or network**
- **www.atsdr.cdc.gov**



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ToxFAQs™ & ToxFAQs™ en Espanol 2003

- **Contains 180 Tox FAQs™ in English and Spanish**
- **Answers frequently asked questions [FAQs] about hazardous substances**
- **Provides search engine to easily cross-reference chemical information**
- **Installs on local hard drive or network**
- **www.atsdr.cdc.gov**

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Supplemental Documents
Databases Searched

- Medline
- CAB (formerly Commonwealth Agricultural database)
- Toxline
- Cancerlit
- Analytical Abstracts
- Occupational Safety and Health (NIOSH)
- NTIS
- BIOSIS
- EMBASE
- Pollution Abstracts
- Enviroline
- Chemical Abstracts
- Food Science and Technology Abstracts
- FEDRIP
- HSDB
- RTECS
- IRIS
- TOMES
- ASTER/AQUIRE
- HAZDAT
- TRI
- Fish Advisories

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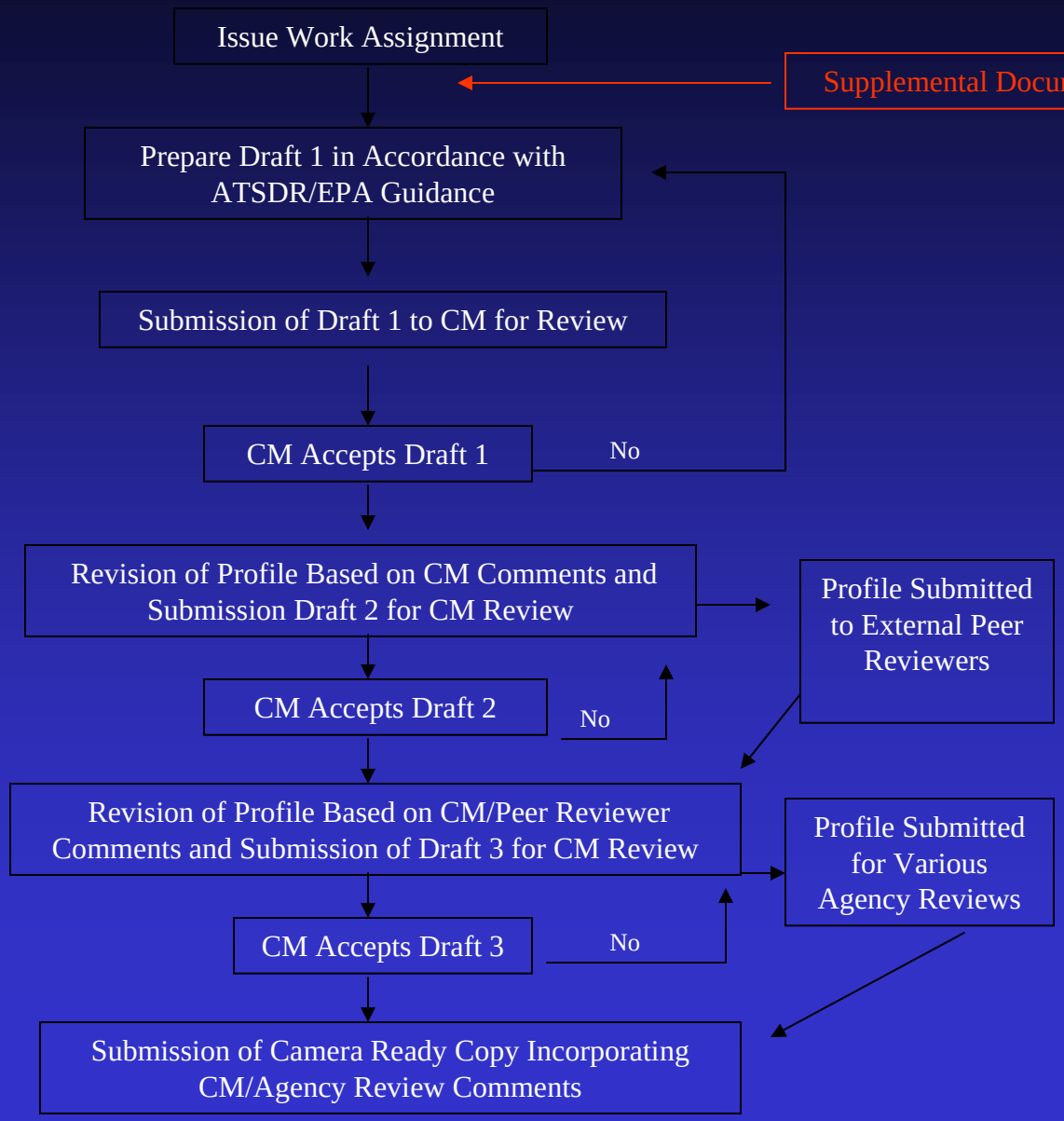
Profile Development Process



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Supplemental Document

Summary Table for Toxicity Studies for Exposure to Nickel - Inhalation

Species/ No. & Sex/ Strain Ref. #	Exposure/ Duration/ Frequency (Specific Route)	Doses	Parameters Monitored	System	NOAEL (mg/m³)	LOAEL Less Serious (mg/m³)	LOAEL Serious (mg/m³)	Reference Chemical Form
ACUTE EXPOSURE								
714 Rat LSE SM, SF (Fischer- 344)	12 days in 16 day period 6 hr/day	0, 0.7, 1.4, 3.1, 6.1, 12.2	LT BW OW HE HP		0.7 F	1.4 F (hyperplasia in bronchial and mediastinal lymph nodes)		NTP 1996c sulfate

Descriptions: Groups of 5 male and 5 female F344/N rats were exposed to 0, 3.5, 7, 15, 30 or 60 nickel sulfate hexahydrate (0, 0.7, 1.4, 3.1, 6.1, 12.2 mg Ni/m3, as calculated by study authors) (MMAD=1.9 mm) for a total of 12 exposures in 16 days (5 days/week, 6 hours/day).

Results: Deaths occurred in 1/5 and 5/5 females exposed to 6.1 and 12.2 mg/m3, respectively and 2/5 males exposed to 12.2 mg/m3. Rats exposed to 1.4 mg/m3 and higher became noticiable thin, had red stained fur around the nose and chin, increased respiratory rates, labored breathing, and decreased activity. Weight gain was significantly lower in all exposed rats as compared to controls ($p<0.05$). Final body weights showed a dose related decrease and were 28% and 40% below controls in males, and 18% and 29% below controls in females exposed at 0.7 and 1.4 mg/m3, respectively. Greater decreases in body weight were observed at the higher concentrations. A significant increase in lung weight was found at all exposure levels in the survivors. In rats that died during the first 5 days, edema and hemorrhage were dominant in the inflammatory response. In rats that died later in the study, cellular infiltration was found and lesions were seen that were similar to those found in the surviving rats. Minimal to moderate lung inflammation was observed in all nickel-exposed rats. The inflammation was centered around terminal airways. Lung inflammation consisted of accumulation of alveolar macrophages and inflammatory cell infiltrate in the alveolar septa. In the terminal airways, necrotic cell debris and fibrin containing inflammatory cells were found. Degeneration of the bronchial epithelium was also observed in all nickel-exposed rats. Atrophy of olfactory epithelium was observed at all exposure concentrations and degeneration of the respiratory epithelium was observed at 3.1 and 6.1 mg/m3. At 1.4 mg/m3, necrotizing lung inflammation was observed. Hyperplasia in the bronchial lymph nodes was observed in males exposed to 3.1 mg/m3 and females exposed to 1.4 mg/m3. Lymphoid depletion in the lymph nodes, thymus, and spleen, and degeneration of the testes was also observed but these effects were considered secondary to the decrease in body weight.

Comments: These data are also reported in Benson et al. 1988 and Dunnick et al. 1988

694 Mouse LSE 80-160F (CD-1)	2 hr	0, 0.288, 0.292, 0.369, 0.499, 0.510	CS BI		0.369 F	0.499 F (increased susceptibility to Streptococcal infection)		Adkins et al. 1979 chloride

Descriptions: Groups of 80-160 CD-1 mice were exposed to 0, 0.288, 0.292, 0.369, 0.499, or 0.510 mg Ni/m3 as nickel chloride (86-96% of particles <1.4 mm diameter) for 2 hours. Immediately or 24 hours after exposure the mice were infected with Streptococci pyogenes

Results: An increase in mortality from Streptococcal infection was observed in the mice exposed to 0.499 mg Ni/m3 and infected 24 hours after termination. No difference in mortality was noted when the mice were infected immediately after nickel exposure to 0.510 mg/m3 or at lower exposure levels.

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Supplemental Document Information

- NUMBER OF ANIMALS
- SPECIES/STRAIN
- EXPOSURE DURATION
- ROUTE OF EXPOSURE
- PARAMETERS MONITORED
- DOSES
- NOAEL/LOAEL VALUES
- CALCULATIONS
- STUDY DESCRIPTION
- COMMENTS

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Levels of Significant Exposure Table

Table 2-1. Levels of Significant Exposure to Benzene - Inhalation

Key to figure[a]	Species/ (strain)	Exposure/ duration/ frequency	System	NOAEL (ppm)	LOAEL: Less serious (ppm)	LOAEL: Serious (ppm)	Reference
	ACUTE EXPOSURE						
	Death						
1	Human	1 d 5-10 min				20000 (death)	Flury 1928
2	Rat (Sprague-Dawley)	4 hr				13700 (LC_{50})	Drew and Fouts 1974
3	Rat (NS)	4 hr				16000 (4/6 died)	Smyth et al. 1962
4	Rabbit (NS)	3.7-36.2 min				45000 (death in 36.2 min)	Carpenter et al. 1944
	Systemic						
5	Human	1-21 d 2.5 - 8 hr/d	Resp		60 M (mucous membrane irritation, dyspnea)		Midzenski et al. 1992
			Hemato			62 M (leukopenia, anemia, thrombocytopenia, MCV elevation)	
			Dermal		60 M (skin irritation)		
6	Rat (Sprague-Dawley)	Gd 6-15 6 hr/d	Bd Wt	300 F	2200 F (decreased maternal body weight)		Green et al. 1978
7	Rat (Sprague-Dawley)	Gd6 -15 7 hr/d	Bd Wt	10 F	50 F (decreased maternal body weight and weight gain)		Kuna and Kapp 1981
8	Rat (Wistar)	7 d 8 hr/d	Hemato	50 F	100 F (leukopenia)		Li et al. 1986
9	Rat (Wistar)	15 min	Cardio			3626 M (ventricular arrhythmia)	Mapes et al. 1990

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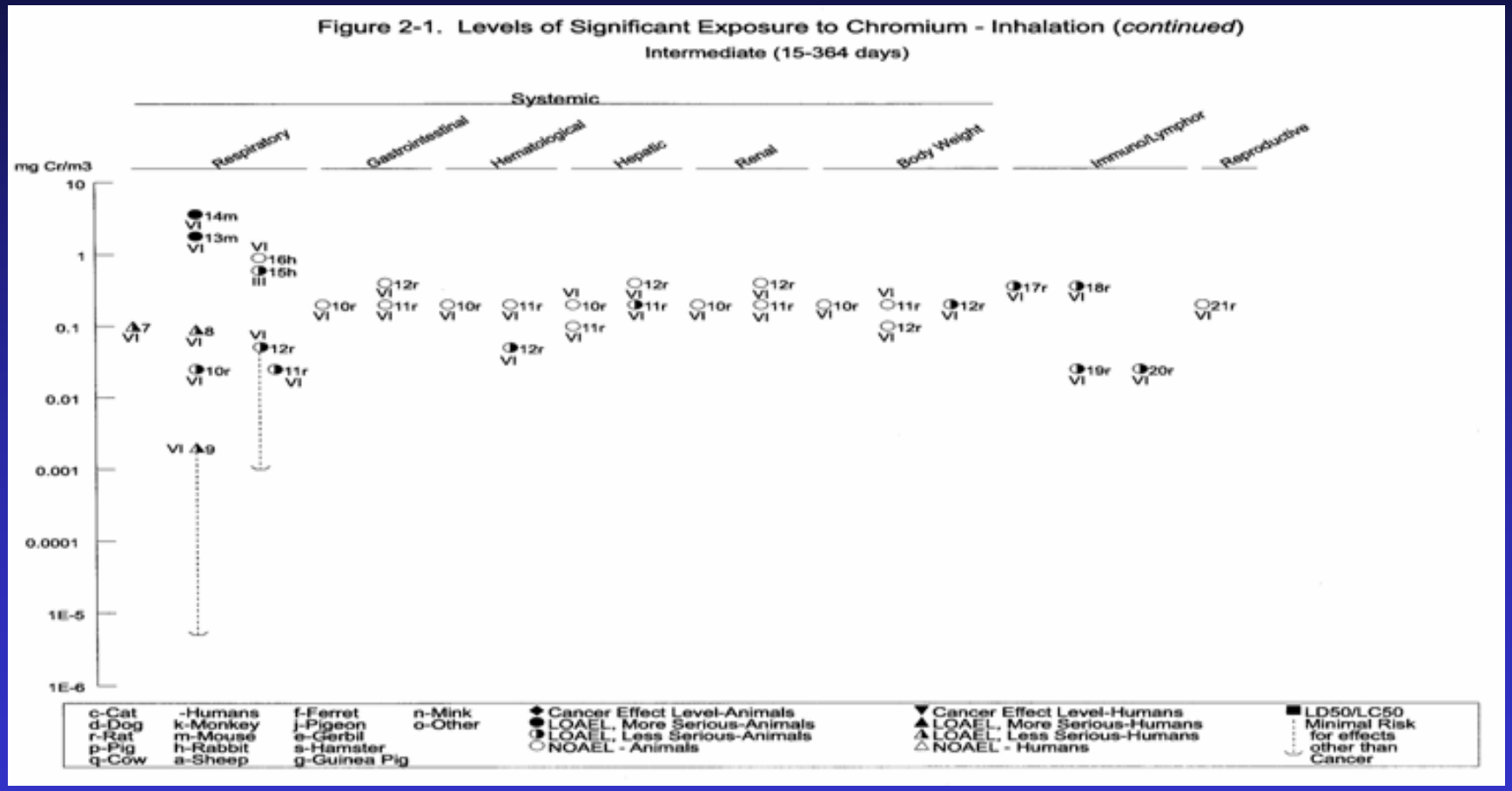
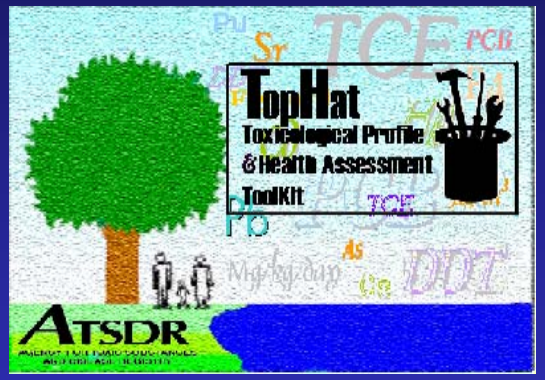
Levels of Significant Exposure Figure



Database Support

HazDat



IRIS
Integrated Risk Information System

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